Chapter 43
Generalizations in Mathematical Epidemiology

Using Computer Algebra and Intuitive Mechanized Reasoning

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Abstract We are concerned by imminent future problems caused by biological dangers, here we think of a way to solve them. One of them is analyzing endemic models, for this we make a study supported by Computer Algebra Systems (CAS) and Mechanized Reasoning (MR). Also we show the advantages of the use of "CAS" and "MR" to obtain in that case, an epidemic threshold theorem. We prove a previously obtained theorem for S^nIR endemic model. Moreover using "CAS+MR" we obtain a new epidemic threshold theorem for the S^nI^mR epidemic model and for the staged progressive SI^mR model. Finally we discuss the relevance of the theorems and some future applications.

1 Introduction

At the moment, we are at the edge of a possible biological problem. Some people say that the nineteenth century was the century of chemistry, the twentieth was the century of physics, and they say that the twenty-first will be the century of biology. If we think, the advances in the biological field in the recent years have been incredible, and like the physics and its atomic bomb, with biology could create global epidemics diseases. Also the climate change could produce a new virus better than the existing virus, creating an atmosphere of panic. For these reasons and others, we think in a solution using mathematical models with computer algebra and mechanized reasoning. Specifically we consider the SIR (Susceptible-Infective-Removed) model, with differential susceptibility and multiple kinds of infected individuals. The objective is to derive three epidemic threshold

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theorems by using the algorithm MKNW given in [1] and a little bit of mechanized reasoning.

Briefly the MKNW runs on: Initially we have a system of ordinary non-lineal differential equations **S**, whose coefficients are polynomial. We start setting all derivates to zero for finding equilibrium; we solve the system finding the equilibrium point **T**. Then we compute the Jacobian **Jb** for the system **S** and replace **T** in **S**. We compute the eigenvalues for **Jb**; from the eigenvalues we obtain the stability conditions when each eigenvalue is less than zero. Finally we obtain the reproductive number for the system **S** in the particular cases. Using deductive reasoning we obtain some theorems based on the particular cases.

The MKNW algorithm is not sufficient to prove the threshold theorems that will be considered here and for this reason, it is necessary to use some form of mechanized reasoning, specifically some strategy of mechanized induction.

The threshold theorem that we probe in Section 2 was originally presented in [2] using only pen and paper and human intelligence. A first contribution of this paper is a mechanized derivation of such theorem using CAS.

The threshold theorem to be proved in Section 3 is original and some particular cases of this theorem were previously considered via CAS in [3, 4] and without CAS in [5].

The threshold theorem to be proved in Section 4 is original and similar models were before considered without CAS in [6].

2 CA And MR Applied to the S^NIR Epidemic Model

We introduce the system for the S^nIR epidemic model, which has n groups of susceptible individuals and which is described by the next system of Eq. [2]:

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t} X_i(t) &= \mu(p_i X_0 - X_i(t)) - \lambda_i X_i(t) \\
\frac{\mathrm{d}}{\mathrm{d}t} Y(t) &= \sum_{k=1}^{n} \lambda_k X_k(t) - (\mu + \gamma + \delta) Y(t) \\
\frac{\mathrm{d}}{\mathrm{d}t} Z(t) &= \gamma Y(t) - (\mu + \varepsilon) Z(t)
\end{aligned} \tag{1}$$

we define the rate of infection as:

$$\lambda_i = \alpha_i \beta \eta Y(t) \tag{2}$$

and we define p_i as follow:

$$\sum_{i=1}^{n} p_i = 1 \tag{3}$$

This is a system with $(n + 2)$ equations and each previous constant is defined like it is shown:

μ is the natural death rate.
γ is the rate at which infectives are removed or become immune.
δ is the disease-induced mortality rate for the infectives.
ε is the disease-induced mortality rate for removed individuals.
α_i is the susceptibility of susceptible individuals.
β is the infectious rate of infected individuals.
η is the average number of contacts per individual.

Each function or group is defined as follow:

$X_i(t)$ are the n groups of susceptible in the time equal t
$Y(t)$ is the group of infectives in the time equal t.
$Z(t)$ is the group of removed in the time equal t.

2.1 The Standard SIR Model

As a particular case we analyze the standard SIR model [7] which has just one group of susceptible and is described in the next equation system:

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}X_1(t) &= \mu(p_1X_0 - X_1(t)) - \lambda_1X_1(t)\\ \frac{\mathrm{d}}{\mathrm{d}t}Y(t) &= \lambda_1X_1(t) - (\mu + \gamma + \delta)Y(t)\\ \frac{\mathrm{d}}{\mathrm{d}t}Z(t) &= \gamma Y(t) - (\mu + \varepsilon)Z(t)\end{aligned} \tag{4}$$

In the infection-free equilibrium there is no variation in time. So the derivates are canceled and the solution for the previous system, it's given by:

$$X_1 = p_1X_0, Y = 0 \tag{5}$$

After, we generate the Jacobian matrix for the equations system:

$$\begin{bmatrix} -\mu - \alpha_1\eta\beta Y & -\alpha_1\eta X_1\beta \\ -\alpha_1\eta\beta Y & \alpha_1\eta X_1\beta - \mu - \gamma - \delta \end{bmatrix}, \tag{6}$$

we substitute the solution (5) in the Jacobian:

$$\begin{bmatrix} -\mu & -\alpha_1\eta p_1X_0\beta \\ 0 & \alpha_1\eta p_1X_0\beta - \mu - \gamma - \delta \end{bmatrix} \tag{7}$$

Now, we find the eigenvalues for the previous matrix:

$$-\mu, \alpha_1 \eta p_1 X_0 \beta - \mu - \gamma - \delta \tag{8}$$

and its corresponding stability condition is:

$$\alpha_1 \eta p_1 X_0 \beta - \mu - \gamma - \delta < 0 \tag{9}$$

this can be rewritten as:

$$\frac{\alpha_1 \eta p_1 X_0 \beta}{\mu + \gamma + \delta} < 1 \tag{10}$$

using the next expression:

$$R_0 < 1 \tag{11}$$

Finally we find the basic reproduction number which it represents the condition of equilibrium:

$$R_0 = \frac{\alpha_1 \eta p_1 X_0 \beta}{\mu + \gamma + \beta} \tag{12}$$

2.2 The S^2IR Model

As another particular case we analyze the S^2IR model where there are two groups of susceptible and the equations for this system are:

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t} X_1(t) &= \mu(p_1 X_0 - X_1(t)) - \lambda_1 X_1(t) \\
\frac{\mathrm{d}}{\mathrm{d}t} X_2(t) &= \mu(p_2 X_0 - X_2(t)) - \lambda_2 X_2(t) \\
\frac{\mathrm{d}}{\mathrm{d}t} Y(t) &= \lambda_1 X_1(t) + \lambda_2 X_2(t) - Y(t)\mu - \gamma Y(t) - Y(t)\delta \\
\frac{\mathrm{d}}{\mathrm{d}t} Z(t) &= \gamma Y(t) - (\mu + \varepsilon) Z(t)
\end{aligned} \tag{13}$$

Initially we find the infection-free equilibrium solution for the previous system:

$$X_1 = p_1 X_0, X_2 = p_2 X_0, Y = 0 \tag{14}$$

Equally we generate the Jacobian matrix for the equations system and substituting the infection-free equilibrium point in the Jacobian:

$$\begin{bmatrix} -\mu & 0 & -\alpha_1 \eta p_1 X_0 \beta \\ 0 & -\mu & -\alpha_2 \eta p_2 X_0 \beta \\ 0 & 0 & \alpha_1 \eta p_1 X_0 \beta + \alpha_2 \eta p_2 X_0 \beta - \mu - \gamma - \delta \end{bmatrix} \tag{15}$$

we find the eigenvalues for the previous Jacobian,

$$-\mu, -\mu, \alpha_1 \eta p_1 X_0 \beta + \alpha_2 \eta p_2 X_0 \beta - \mu - \gamma - \delta \tag{16}$$

and the corresponding stability condition is:

$$\alpha_1 \eta p_1 X_0 \beta + \alpha_2 \eta p_2 X_0 \beta - \mu - \gamma - \delta < 0 \tag{17}$$

this can be rewritten as:

$$\frac{\alpha_1 \eta p_1 X_0 \beta + \alpha_2 \eta p_2 X_0 \beta}{\mu + \gamma + \delta} < 1 \tag{18}$$

also it can be written using (11) as:

$$R_0 = \frac{\alpha_1 \eta p_1 X_0 \beta + \alpha_2 \eta p_2 X_0 \beta}{\mu + \gamma + \delta} \tag{19}$$

this is the basic reproductive number for S^2IR model.

2.3 The S^3IR, The S^4IR and S^5IR Models

Here we show the S^3IR, the S^4IR and S^5IR models where there are three, four and five groups of susceptibles, respectively. With these models we do the same process, and we only show the basic reproductive number.

$$R_0 = \frac{\alpha_1 \eta p_1 X_0 \beta + \alpha_2 \eta p_2 X_0 \beta + \alpha_3 \beta \eta p_3 X_0}{\mu + \gamma + \delta} \tag{20}$$

this is the basic reproductive number for S^3IR model.

$$R_0 = \frac{\alpha_1 \eta p_1 X_0 \beta + \alpha_2 \eta p_2 X_0 \beta + \alpha_3 \beta \eta p_3 X_0 + \alpha_4 \beta \eta p_4 X_0}{\mu + \gamma + \delta} \tag{21}$$

this is the basic reproductive number for S^4IR model.

$$R_0 = \frac{X_0 \beta \eta (\alpha_1 p_1 + \alpha_2 p_2 + \alpha_3 p_3 + \alpha_4 p_4 + \alpha_5 p_5)}{\mu + \gamma + \delta} \tag{22}$$

and this is the basic reproductive number for S^5IR model.

2.4 The S^nIR Model

Theorem. *For the equations system given by (1). The infection-free equilibrium is locally stable if $R_0 < 1$, and is unstable if $R_0 > 1$, where:*

$$R_0 = \frac{X_0 \beta \eta \left(\sum_{i=1}^{n} \alpha_i p_i \right)}{\mu + \gamma + \delta} \tag{23}$$

We can probe the theorem looking the inequalities corresponding to stability conditions for each system previously considered, we have listed in the Fig. 1. Using mechanized induction we obtain the general expression for the stability conditions for a system with (n + 2) equations.

$$\frac{X_0 \beta \eta \left(\sum_{i=1}^{n} \alpha_i p_i \right)}{\mu + \gamma + \delta} < 1 \tag{24}$$

We can represent into a schematic diagram, the deductive reasoning using "MR".

Here we have an idea for the MR, it finds the similar components in each item and it has a viewer or a detector that find the sequential form for the dissimilar parts. It is just an idea, we believe this system have to be improved by the scientific community.

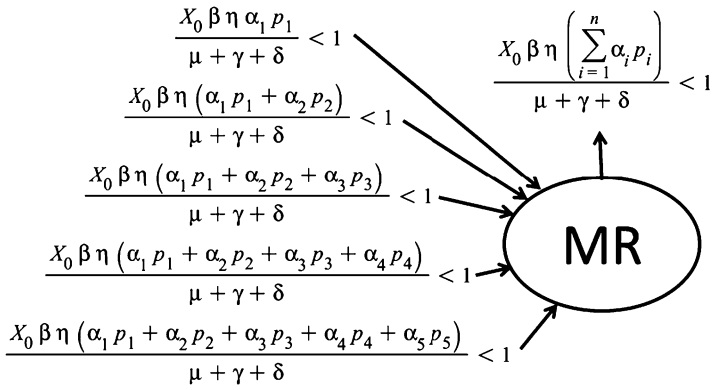

Fig. 1 Inductive mechanized reasoning for the S^nIR Model

3 CA and MR Applied to the S^NI^MR Epidemic Model

The S^nI^mR epidemic model is made by a group of equations which has n groups of susceptible individuals and m groups of infected people, this system is illustrated in the next equations:

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}X_i(t) &= \mu(p_iX_0 - X_i(t)) - \alpha_i\eta\left(\sum_{i=1}^{m}\beta_jY_j(t)\right)X_i(t)\\
\frac{\mathrm{d}}{\mathrm{d}t}Y_j(t) &= \eta\beta_jY_j(t)\left(\sum_{i=1}^{n}\alpha_iX_i(t)\right) - (\mu+\gamma+\delta)Y_j(t)\\
\frac{\mathrm{d}}{\mathrm{d}t}Z(t) &= \gamma Y_j(t) - (\mu+\varepsilon)Z(t)
\end{aligned} \tag{25}$$

p_i is defined in (3). This is a system with (n + m + 1) equations and each constant were defined in the last model.

3.1 The SI^2R Model

Like in all cases, we analyze a particular case with one group of susceptibles and two groups of infectives. The following equations describe this case:

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}X_1(t) &= \mu(p_1X_0 - X_1(t)) - \alpha_1\eta\left(\sum_{j=1}^{2}\beta_jY_j(t)\right)X_1(t)\\
\frac{\mathrm{d}}{\mathrm{d}t}Y_1(t) &= \eta\beta_1Y_1(t)\left(\sum_{i=1}^{1}\beta_iX_i(t)\right) - (\mu+\gamma+\delta)Y_1(t)\\
\frac{\mathrm{d}}{\mathrm{d}t}Y_2(t) &= \eta\beta_2Y_2(t)\left(\sum_{i=1}^{1}\alpha_iX_i(t)\right) - (\mu+\gamma+\delta)Y_2(t)\\
\frac{\mathrm{d}}{dt}Z(t) &= \gamma Y_j(t) - (\mu+\varepsilon)Z(t)
\end{aligned} \tag{26}$$

Solving the system for the infection-free equilibrium, we find:

$$Y_1 = 0, Y_2 = 0, X_1 = \frac{\mu p_1X_0}{\mu + \alpha_1\eta\left(\sum_{j=1}^{2}\beta_jY_j\right)} \tag{27}$$

We generate a Jacobian as in the others cases. After, we substitute the infection-free equilibrium point and we find the eigenvalues for the system,

$$-\mu, \alpha_1 \eta p_1 X_0 \beta_1 - \mu - \gamma - \delta, \alpha_1 \eta p_1 X_0 \beta_2 - \mu - \gamma - \delta \tag{28}$$

The stability conditions shall satisfy,

$$\begin{aligned} \alpha_1 \eta p_1 X_0 \beta_2 - \mu - \gamma - \delta < 0 \\ \alpha_1 \eta p_1 X_0 \beta_1 - \mu - \gamma - \delta < 0 \end{aligned} \tag{29}$$

Moreover the inequalities in (29) can be written like the others cases as:

$$\begin{aligned} R_{0,2} = \frac{\alpha_1 \eta p_1 X_0 \beta_2}{\mu + \gamma + \delta} \\ R_{0,1} = \frac{\alpha_1 \eta p_1 X_0 \beta_1}{\mu + \gamma + \delta} \end{aligned} \tag{30}$$

Here, we have the two basic reproductive numbers for SI^2R model.

3.2 The S^2I^2R Model

We analyze a particular case where we have two groups of susceptible and two groups of infective, in addition we solve the system for the infection-free equilibrium and we find:

$$Y_1 = 0, Y_2 = 0, X_1 = \frac{\mu p_1 X_0}{\mu + \alpha_1 \eta \left(\sum_{j=1}^{2} \beta_j Y_j \right)}, X_2 = \frac{\mu p_2 X_0}{\mu + \alpha_2 \eta \left(\sum_{j=1}^{2} \beta_j Y_j \right)} \tag{31}$$

Also we generate a Jacobian; we substitute the infection-free equilibrium point and find the eigenvalues for this system:

$$\begin{aligned} -\mu, -\mu, \alpha_1 \eta p_1 X_0 \beta_1 + \alpha_2 \eta p_2 X_0 \beta_1 - \mu - \gamma - \delta, \alpha_1 \eta p_1 X_0 \beta_2 \\ + \alpha_2 \eta p_2 X_0 \beta_2 - \mu - \gamma - \delta \end{aligned} \tag{32}$$

In like manner that we obtained the last reproductive numbers, we obtain the two basic reproductive numbers for S^2I^2R model:

$$\begin{aligned} R_{0,2} = \frac{\alpha_1 \eta p_1 X_0 \beta_2 + \alpha_2 \eta p_2 X_0 \beta_2}{\mu + \gamma + \delta} \\ R_{0,1} = \frac{\alpha_1 \eta p_1 X_0 \beta_1 + \alpha_2 \eta p_2 X_0 \beta_1}{\mu + \gamma + \delta} \end{aligned} \tag{33}$$

3.3 The S^nI^mR Model

Theorem. *For the equations system given by (25). The infection-free equilibriums are locally stable if the reproductive numbers of infection $R_{0,j} < 1$, and is unstable if $R_{0,j} > 1$, with j from 1 to m, where:*

$$R_{0,j} = \frac{X_0 \eta \left(\sum_{i=1}^{n} \alpha_i p_i \right) \beta_j}{\mu + \gamma + \delta} \tag{34}$$

To prove the theorem, we used mechanized induction starting from the particular results previously obtained in (30) and (33). Finally, we find the general solution for the basic reproductive numbers for the S^nI^mR model according with (Fig. 2).

4 CA and MR Applied to the Staged Progressive SI^MR Epidemic Model

At this moment, we are concerned in the analysis of the staged progressive SI^mR epidemic model. This has m groups of infected; in this case the infection is staged and progressive, which is described by next system:

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}X(t) &= \mu(x_0 - X(t)) - \lambda X(t) \\
\frac{\mathrm{d}}{\mathrm{d}t}Y_1(t) &= \lambda X(t) - (\mu + \gamma_1 + \delta_1)Y_1(t) \\
\frac{\mathrm{d}}{\mathrm{d}t}Y_j(t) &= Y_{j-1}Y_{j-1}(t) - (\mu + \gamma_j + \delta_j)Y_j(t) \\
\frac{\mathrm{d}}{\mathrm{d}t}Z(t) &= \gamma_m Y_m(t) - (\mu + \varepsilon)Z(t)
\end{aligned} \tag{35}$$

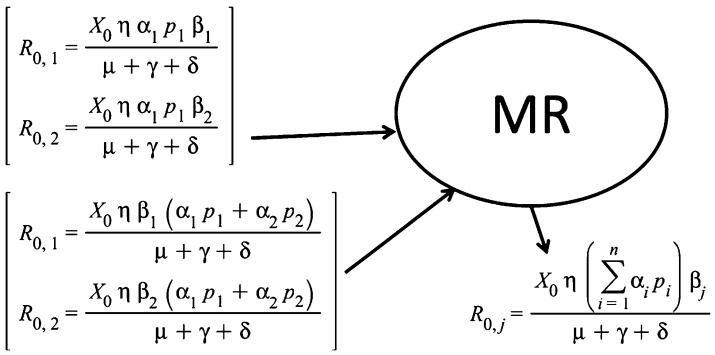

Fig. 2 Inductive mechanized reasoning for the S^nI^mR Model

with the restriction for j is: $2 \leq j \leq m$. And where the rate of infection is:

$$\lambda = \alpha\left(\sum_{j=1}^{m} \beta_j Y_j(t)\right)\eta \tag{36}$$

This is a system with (m + 2) equations and all the constants were described before.

4.1 The Staged Progressive SI^2R Model

Now, we analyze a particular case with one group of susceptible and two groups of infectives. The following equations describe this case:

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}X(t) &= \mu(x_0 - X(t)) - \lambda X(t)\\
\frac{\mathrm{d}}{\mathrm{d}t}Y_1(t) &= \lambda X(t) - (\mu + \gamma_1 + \delta_1)Y_1(t)\\
\frac{\mathrm{d}}{\mathrm{d}t}Y_2(t) &= \lambda_1 Y_1(t) - (\mu + \gamma_2 + \delta_2)Y_2(t)\\
\frac{\mathrm{d}}{\mathrm{d}t}Z(t) &= \lambda_2 Y_2(t) - (\mu + \varepsilon)Z(t)
\end{aligned} \tag{37}$$

Solving the system for the infection-free equilibrium, we find:

$$X = \frac{\mu x_0}{\mu + \alpha\eta\beta_1 Y_1 + \alpha\eta\beta_2 Y_2}, Y_1 = 0, Y_2 = 0 \tag{38}$$

We generate a Jacobian coming off the equations system and substituting the infection-free equilibrium point:

$$\begin{vmatrix}
-\mu & -\alpha\eta x_0\beta_1 & -\alpha\eta x_0\beta_2\\
0 & -\alpha\eta x_0\beta_1 - \mu - \gamma_1 - \delta_1 & \alpha\eta x_0\beta_2\\
0 & \gamma_1 & -\mu - \gamma_2 - \delta_2
\end{vmatrix} \tag{39}$$

Now we obtain the characteristic polynomial:

$$\begin{aligned}
&(\lambda + \mu)(\lambda^2 + 2\lambda\mu + \lambda\gamma_2 + \lambda\delta_2 - \alpha\eta x_0\beta_1\lambda - \alpha\eta x_0\beta_1\mu\\
&- \alpha\eta x_0\beta_1\gamma_2 - \alpha\eta x_0\beta_1\delta_2 + \mu^2 + \mu\gamma_2 + \mu\delta_2 + \gamma_1\lambda\\
&+ \gamma_1\mu + \gamma_1\gamma_2 + \gamma_1\delta_2 + \delta_1\lambda + \delta_1\gamma_2 + \delta_1\delta_2\\
&- \alpha\eta x_0\beta_2\gamma_1
\end{aligned} \tag{40}$$

From this polynomial, we obtain the basic reproduction number using the Routh-Hurwitz theorem:

$$R_0 = \frac{x_0\alpha\eta(\beta_1\delta_2 + \beta_1\mu + \beta_1\gamma_2 + \beta_2\gamma_1)}{(\mu + \gamma_2 + \delta_2)(\mu + \gamma_1 + \delta_1)} \tag{41}$$

4.2 The Staged Progressive SI^3R Model

We analyze a particular case with three groups of infectives. We solve this system in the same way that we did in the Section 4.1. For this model the basic reproduction number that we find is:

$$\begin{aligned} R_0 = (&x_0\alpha\eta(\beta_1\delta_2\mu + \beta_1\delta_2\lambda_3 + \beta_1\mu\lambda_3 + \beta_1\gamma_2\mu + \beta_1\gamma_2\gamma_3 \\ &+\beta_1\gamma_2\delta_3 + \beta_1\mu^2 + \beta_1\delta_2\delta_3 + \gamma_1\beta_2\mu + \gamma_1\beta_2\gamma_3 + \gamma_1\beta_2\delta_3 \\ &+\gamma_1\beta_3\gamma_2 + \beta_1\mu\delta_3))/((\mu + \gamma_3 + \delta_3)(\mu + \gamma_2 + \delta_2)(\mu \\ &+\gamma_1 + \delta_1)) \end{aligned} \tag{42}$$

4.3 Staged Progressive SI^mR Model

Theorem. *For the equations system given by (35). The infection-free equilibrium is locally stable if the reproductive numbers of infection $R_0 < 1$, and is unstable if $R_0 > 1$, with j from 1 to m, where:*

$$R_0 = \frac{x_0\alpha\eta\left(\sum_{j-1}^{m}\beta_j\prod_{k=1}^{j-1}\gamma_k\prod_{l=j+1}^{m}(\mu + \gamma_l + \delta_l)\right)}{\prod_{l=1}^{m}(\mu + \gamma_l + \delta_l)} \tag{43}$$

To prove the theorem, we used mechanized induction starting from the particular results previously obtained. To conclude, we find the general solution for the basic reproductive numbers for the Staged Progressive SI^mR model according with (Fig. 3).

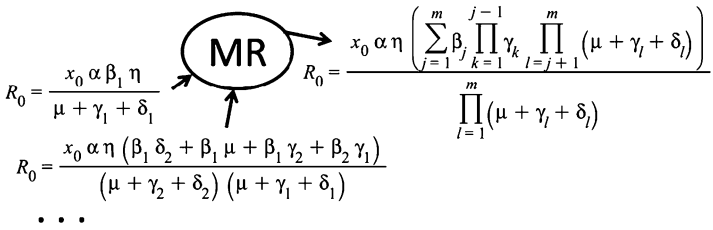

Fig. 3 Inductive mechanized reasoning for the staged progressive SI^mR Model

5 Conclusions

We finally obtain three theorems which can help us to demonstrate that CAS+MR are important tools for solving problems in every situation that mathematics could model. The theorems are useful to make strategies to fight against epidemic diseases in the future biological dangers.

Due to use CAS, in our case "Maple 11", we can proceed to solve the mathematical problem and we can obtain results very fast that without them could take us too much time.

The use of CAS+MR can help in teaching and learning the mathematics to engineering, whose don't have time and need to give quickly solutions. It can be implemented in engineer programs.

Through the MR we already found the general forms for the infection free equilibrium, we can see the importance of developing software it can do the mechanized reasoning automatically.

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